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EXPERIMENTAL GASTRIC ULCERS INDUCED BY IMMOBILIZATION AND ELECTRIC SHOCK OF RATS AND THEIR PHARMACOTHERAPY

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16. Abstract

The most marked preventive effect in the development of experimentally induced gastric ulcers in rats was displayed by agents capable of blocking the ascending activating system of the reticular formation. Sympathetic fibers, which disrupt the trophism of the gastric wall, form the efferent portion of the reflex arc. Gastric secretion does not appear to be the primary cause of ulceration.

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EXPERIMENTAL GASTRIC ULCERS INDUCED BY IMMOBILIZATION AND ELECTRIC SHOCK OF RATS AND THEIR PHARMACOTHERAPY

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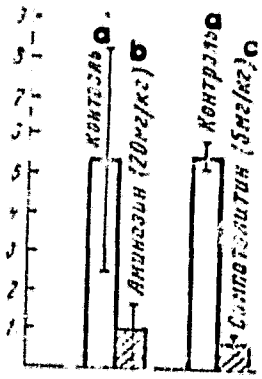
The goal of this work was the pharmacological analysis of the mechanism of development of experimental gastric ulcers, induced in rats by combined immobilization of the animals and electric shock for 3 hours [7]. /717*

We used neurotropic agents, which interrupted the reflex arc in various parts of it. The preparations were administered intraperitoneally, 10 min before the start of stimulation with electric current.

It turned out that the number of destructive changes in the stomach wall in tests with the so called central sedatives phenobarbital and amobarbital (100 mg/kg) were 6 and 5 times less than in the control, on the average. Urethane (1 g/kg), chloral hydrate (100 mg/kg) and paraldehyde (3 g/kg), so called cortical sedatives, in doses which induced the side position (seminarcosis), even increased the number of destructive lesions, especially urethane. The central cholinolytic diazyl (3 mg/kg), administered twice, decreased the number of destructive lesions of the stomach mucosa 3.8 times. In tests with aminazine (20 mg/kg), an appreciable preventive effect was observed. The number of destructive changes in test group animals was decreased 5.3 times, compared with the control group (see figure).

Morphine, administered at a dose of 5 mg/kg, which caused complete analgesia did not decrease the rate of destructive lesions, but it considerably reduced their severity. In the test with morphine, there were point erosions of the mucosa without hemorrhage, while distinct ulcerous defects filled with clotted blood were observed in the control. The

*Numbers in the margin indicate pagination in the foreign text.



Effect of aminazine and sympatholytin on formation of gastric ulcers in rats. Column height designates average number of damaged sections in one animal.

Key: a. Control
b. Aminazine (20 mg/kg)
c. Sympatholytin (5 mg/kg)

greatest protective effect was noted with sympatholytin (5 mg/kg), which was administered an hour before the start of electric shock (see figure). The sympatholytic guanethidine (10 mg/kg), which does not block the adrenergic system, also administered an hour before the start of electric shock, had less protective effect: the number of destructive changes in one control animal was 2.4 but, in the test, 1.7. Atropine did not affect the number of destructive changes in the stomach. /718

In comparing the results obtained, it was found that phenobarbital, amobarbital, diazyl and aminazine had the greatest preventive effect, i.e., those compounds which block the conduct of nerve impulses in the ascending activating system of the reticular formations. Meprobamate, which excites the ascending activating system of the reticular formations in the dose we tested (50 mg/kg) [4], increased the lesion frequency. In the mechanism of the preventive effect of the central cholinolytic diazyl, its blocking effect on the m-cholinergic system of the brainstem evidently can play a part. Our tests have shown that diazyl had a pronounced protective effect in the development of experimental gastric ulcers of rats and, at the same doses, it prevented the onset of arecoline tremor in them, while difasil and typhen had such a capacity to a negligible extent and did not protect the stomach mucosa from the development of destructive changes in it.

Aminazine, which proved to be ineffective for the prevention of neurogenic dystrophy induced by trauma of the duodenal region, actively protected the stomach mucosa from destructive lesions in electric shock and immobilization of the animals. This is consistent with the data of [2, 5]. The explanation of this difference in protective effect of aminazine evidently is that, in the generalized irritation induced by

combined immobilization and electric shock, other pathways of the afferent portion of the reflex, than in the irritation of the duodenal region are involved. It can be assumed that aminazine, by blocking the impulses due to stimulation of the exteroceptors, does not have a similar effect in stimulation of the interoceptors of the duodenal region. The explanation of the inadequate protective effect of morphine in the development of experimental gastric ulcers in rats evidently is that, in the doses we used, it did not block the ascending activating system of the reticular formations.

Analysis of the effect of peripheral neurotropic agents permits the assumption that the efferent portion of the reflex arc, which disrupted trophism, are the sympathetic fibers. The results of our tests with sympatholytin, confirmed by data obtained in neurogenic dystrophies connected with trauma of the duodenal region, indicate this. The blocking of the peripheral adrenergic systems by sympatholytin most effectively prevented the development of destructive changes. The sympatholytic guanethidine had less preventive effect. This probably is explained by the difference in the mechanisms of their sympatholytic actions: guanethidine, which, as is known, decreases the catecholamine concentration in the tissues and organs and decreases the output of the sympathetic mediator [3], is itself capable of causing gastric ulcers in rats at large doses, as was shown by D.G. Rozin. Blocking of the peripheral /719
cholinergic synapses and complete depression of gastric secretions by atropine, at a dose of 1 mg/kg, did not prevent the development of destructive lesions. This confirms the fact that the increased gastric secretions is not the leading factor in the mechanism of development of experimental gastric ulcers in rats, which was pointed out long ago in work performed under the supervision of S.V. Anichkov [8]. This has been confirmed in the work of American authors [5, 1].

Conclusions

1. In the development of destructive lesions in the stomach mucosa, the central neurotropic agents which block the conduct of nerve impulses in the ascending activating system of the reticular formations

had the greatest preventive effect.

2. The efferent portion of the reflex arc, which disrupted trophism in the stomach wall, are the sympathetic fibers.

3. Increased gastric secretion is not the leading factor in the mechanism of development of experimental gastric ulcers, induced in rats by combined immobilization and electric shock.

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